

HOME COPY

PCT

REQUEST

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.

For Filing Office use only

PCT/US 00/08871
International Application No.

04 APR 2000 (04.04.00)

International Filing Date

PCT INTERNATIONAL

Name of Applicant: "COLOR ACCESS, INC." International Application

Applicant's or agent's file reference 2870/250
(if desired) (12 characters maximum)

Box No. I TITLE OF INVENTION

COMPOSITION FOR IMPROVING SKIN LIPID BARRIER FUNCTION

Box No. II APPLICANT

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

COLOR ACCESS, INC.
7 Coporate Center Drive
Melville, New York 11747
US

☐ This person is also inventor.

Telephone No.

Facsimile No.

Teleprinter No.

State (that is, country) of nationality:
USState (that is, country) of residence:
US

This person is applicant for the purposes of: ☐ all designated States ☒ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

MAES, Daniel H.
279A Nassau Road
Huntington, New York 11743
US

This person is:

☐ applicant only☒ applicant and inventor☐ inventor only (If this check-box is marked, do not fill in below.)State (that is, country) of nationality:
FRState (that is, country) of residence:
US

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☒ the United States of America only ☐ the States indicated in the Supplemental Box

☒ Further applicants and/or (further) inventors are indicated on a continuation sheet.

Box No. IV AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE

The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as:



agent



common representative

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)

TSEVDOS, Estelle J.
Kenyon & Kenyon
One Broadway
New York, New York 10004
US

Telephone No.
212-425-7200Facsimile No.
212-425-5288

Teleprinter No.

☐ Address for correspondence: Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.

Continuation of Box No. III FURTHER APPLICANTS AND/OR (FURTHER) INVENTOR(S)

If none of the following sub-boxes is used, this sheet is not to be included in the request.

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

ANDERSON, Jon
3838 Briarpatch Circle
Galesburg, Michigan 49053
US

This person is:

- ☐ applicant only
☒ applicant and inventor
☐ inventor only (If this check-box is marked, do not fill in below.)

State (that is, country) of nationality:
US

State (that is, country) of residence:
US

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☒ the United States of America only ☐ the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

MARENUS, Kenneth D.
62 McCulloch Drive
Dix Hills, New York 11746
US

This person is:

- ☐ applicant only
☒ applicant and inventor
☐ inventor only (If this check-box is marked, do not fill in below.)

State (that is, country) of nationality:
US

State (that is, country) of residence:
US

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☒ the United States of America only ☐ the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

MAMMONE, Thomas
4 Spencer Street
Farmingdale, New York 11735
US

This person is:

- ☐ applicant only
☒ applicant and inventor
☐ inventor only (If this check-box is marked, do not fill in below.)

State (that is, country) of nationality:
US

State (that is, country) of residence:
US

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☒ the United States of America only ☐ the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

FTHENAKIS, Christina G.
9 Lucille Lane
Dix Hills, New York 11746
US

This person is:

- ☐ applicant only
☒ applicant and inventor
☐ inventor only (If this check-box is marked, do not fill in below.)

State (that is, country) of nationality:
US

State (that is, country) of residence:
US

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☒ the United States of America only ☐ the States indicated in the Supplemental Box

☐ Further applicants and/or (further) inventors are indicated on another continuation sheet.

Box No. V DESIGNATION OF STATES

The following designations are hereby made under Rule 4.9(a) (mark the applicable check-boxes; at least one must be marked):

Regional Patent

- ☒ **AP ARIPO Patent:** GH Ghana, GM Gambia, KE Kenya, LS Lesotho, MW Malawi, SD Sudan, SL Sierra Leone, SZ Swaziland, TZ United Republic of Tanzania, UG Uganda, ZW Zimbabwe, and any other State which is a Contracting State of the Harare Protocol and of the PCT
- ☒ **EA Eurasian Patent:** AM Armenia, AZ Azerbaijan, BY Belarus, KG Kyrgyzstan, KZ Kazakhstan, MD Republic of Moldova, RU Russian Federation, TJ Tajikistan, TM Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT
- ☒ **EP European Patent:** AT Austria, BE Belgium, CH and LI Switzerland and Liechtenstein, CY Cyprus, DE Germany, DK Denmark, ES Spain, FI Finland, FR France, GB United Kingdom, GR Greece, IE Ireland, IT Italy, LU Luxembourg, MC Monaco, NL Netherlands, PT Portugal, SE Sweden, and any other State which is a Contracting State of the European Patent Convention and of the PCT
- ☒ **OA OAPI Patent:** BF Burkina Faso, BJ Benin, CF Central African Republic, CG Congo, CI Côte d'Ivoire, CM Cameroon, GA Gabon, GN Guinea, GW Guinea-Bissau, ML Mali, MR Mauritania, NE Niger, SN Senegal, TD Chad, TG Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT (if other kind of protection or treatment desired, specify on dotted line)

National Patent (if other kind of protection or treatment desired, specify on dotted line):

- | | |
|--|--|
| <input checked="" type="checkbox"/> AE United Arab Emirates | <input checked="" type="checkbox"/> LR Liberia |
| <input checked="" type="checkbox"/> AL Albania | <input checked="" type="checkbox"/> LS Lesotho |
| <input checked="" type="checkbox"/> AM Armenia | <input checked="" type="checkbox"/> LT Lithuania |
| <input checked="" type="checkbox"/> AT Austria | <input checked="" type="checkbox"/> LU Luxembourg |
| <input checked="" type="checkbox"/> AU Australia | <input checked="" type="checkbox"/> LV Latvia |
| <input checked="" type="checkbox"/> AZ Azerbaijan | <input checked="" type="checkbox"/> MA Morocco |
| <input checked="" type="checkbox"/> BA Bosnia and Herzegovina | <input checked="" type="checkbox"/> MD Republic of Moldova |
| <input checked="" type="checkbox"/> BB Barbados | <input checked="" type="checkbox"/> MG Madagascar |
| <input checked="" type="checkbox"/> BG Bulgaria | <input checked="" type="checkbox"/> MK The former Yugoslav Republic of Macedonia |
| <input checked="" type="checkbox"/> BR Brazil | |
| <input checked="" type="checkbox"/> BY Belarus | <input checked="" type="checkbox"/> MN Mongolia |
| <input checked="" type="checkbox"/> CA Canada | <input checked="" type="checkbox"/> MW Malawi |
| <input checked="" type="checkbox"/> CH and LI Switzerland and Liechtenstein | <input checked="" type="checkbox"/> MX Mexico |
| <input checked="" type="checkbox"/> CN China | <input checked="" type="checkbox"/> NO Norway |
| <input checked="" type="checkbox"/> CR Costa Rica | <input checked="" type="checkbox"/> NZ New Zealand |
| <input checked="" type="checkbox"/> CU Cuba | <input checked="" type="checkbox"/> PL Poland |
| <input checked="" type="checkbox"/> CZ Czech Republic | <input checked="" type="checkbox"/> PT Portugal |
| <input checked="" type="checkbox"/> DE Germany | <input checked="" type="checkbox"/> RO Romania |
| <input checked="" type="checkbox"/> DK Denmark | <input checked="" type="checkbox"/> RU Russian Federation |
| <input checked="" type="checkbox"/> DM Dominica | <input checked="" type="checkbox"/> SD Sudan |
| <input checked="" type="checkbox"/> EE Estonia | <input checked="" type="checkbox"/> SE Sweden |
| <input checked="" type="checkbox"/> ES Spain | <input checked="" type="checkbox"/> SG Singapore |
| <input checked="" type="checkbox"/> FI Finland | <input checked="" type="checkbox"/> SI Slovenia |
| <input checked="" type="checkbox"/> GB United Kingdom | <input checked="" type="checkbox"/> SK Slovakia |
| <input checked="" type="checkbox"/> GD Grenada | <input checked="" type="checkbox"/> SL Sierra Leone |
| <input checked="" type="checkbox"/> GE Georgia | <input checked="" type="checkbox"/> TJ Tajikistan |
| <input checked="" type="checkbox"/> GH Ghana | <input checked="" type="checkbox"/> TM Turkmenistan |
| <input checked="" type="checkbox"/> GM Gambia | <input checked="" type="checkbox"/> TR Turkey |
| <input checked="" type="checkbox"/> HR Croatia | <input checked="" type="checkbox"/> TT Trinidad and Tobago |
| <input checked="" type="checkbox"/> HU Hungary | <input checked="" type="checkbox"/> TZ United Republic of Tanzania |
| <input checked="" type="checkbox"/> ID Indonesia | <input checked="" type="checkbox"/> UA Ukraine |
| <input checked="" type="checkbox"/> IL Israel | <input checked="" type="checkbox"/> UG Uganda |
| <input checked="" type="checkbox"/> IN India | <input checked="" type="checkbox"/> US United States of America |
| <input checked="" type="checkbox"/> IS Iceland | |
| <input checked="" type="checkbox"/> JP Japan | <input checked="" type="checkbox"/> UZ Uzbekistan |
| <input checked="" type="checkbox"/> KE Kenya | <input checked="" type="checkbox"/> VN Viet Nam |
| <input checked="" type="checkbox"/> KG Kyrgyzstan | <input checked="" type="checkbox"/> YU Yugoslavia |
| <input checked="" type="checkbox"/> KP Democratic People's Republic of Korea | <input checked="" type="checkbox"/> ZA South Africa |
| | <input checked="" type="checkbox"/> ZW Zimbabwe |
| <input checked="" type="checkbox"/> KR Republic of Korea | Check-boxes reserved for designating States which have become party to the PCT after issuance of this sheet: |
| <input checked="" type="checkbox"/> KZ Kazakhstan | <input checked="" type="checkbox"/> DZ Algeria |
| <input checked="" type="checkbox"/> LC Saint Lucia | <input checked="" type="checkbox"/> AG Antigua and Barbuda |
| <input checked="" type="checkbox"/> LK Sri Lanka | |

Precautionary Designation Statement: In addition to the designations made above, the applicant also makes under Rule 4.9(b) all other designations which would be permitted under the PCT except any designation(s) indicated in the Supplemental Box as being excluded from the scope of this statement. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. (Confirmation (including fees) must reach the receiving Office within the 15-month time


Box No. VI PRIORITY CLAIM		<input type="checkbox"/> Further priority claim indicated in the Supplemental Box.		
Filing date of earlier application (day/month/year)	Number of earlier application	Where earlier application is:		
		national application: country	regional application:* regional Office	international application: receiving Office
item (1)				
item (2)				
item (3)				

☐ The receiving Office is requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) (only if the earlier application was filed with the Office which for the purposes of the present international application is the receiving Office) identified above as item(s):

* Where the earlier application is an ARIPO application, it is mandatory to indicate in the Supplemental Box at least one country party to the Paris Convention for the Protection of Industrial Property for which that earlier application was filed (Rule 4.10(b)(ii)). See Supplemental Box.

Box No. VII INTERNATIONAL SEARCHING AUTHORITY			
Choice of International Searching Authority (ISA) (if two or more International Searching Authorities are competent to carry out the international search, indicate the Authority chosen; the two-letter code may be used):	Request to use results of earlier search; reference to that search (if an earlier search has been carried out by or requested from the International Searching Authority):		
ISA/EP	Date (day/month/year)	Number	Country (or regional Office)

Box No. VIII CHECK LIST: LANGUAGE OF FILING	
This international application contains the following number of sheets: request : 4 description (excluding sequence listing part) : 12 claims : 4 abstract : 1 drawings : sequence listing part of description : Total number of sheets : 21	This international application is accompanied by the item(s) marked below: 1. <input checked="" type="checkbox"/> fee calculation sheet 2. <input type="checkbox"/> separate signed power of attorney 3. <input checked="" type="checkbox"/> copy of general power of attorney; reference number, if any: 4. <input type="checkbox"/> statement explaining lack of signature 5. <input type="checkbox"/> priority document(s) identified in Box No. VI as item(s): 6. <input type="checkbox"/> translation of international application into (language): 7. <input type="checkbox"/> separate indications concerning deposited microorganism or other biological material 8. <input type="checkbox"/> nucleotide and/or amino acid sequence listing in computer readable form 9. <input type="checkbox"/> other (specify):
Figure of the drawings which should accompany the abstract:	Language of filing of the international application: English

Box No. IX SIGNATURE OF APPLICANT OR AGENT
Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the request). <div style="text-align: center;">  <u>by: Mary C. Weiner Reg. No. 30,333</u> Estelle J. Tsevdos Agent for Applicants </div>

For receiving Office use only		(04.04.00)
1. Date of actual receipt of the purported international application:	528 Rec'd PCT/PTO 04 APR 2000	
3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application:		
4. Date of timely receipt of the required corrections under PCT Article 11(2):		
5. International Searching Authority (if two or more are competent): ISA/EP	6. <input type="checkbox"/> Transmittal of search copy delayed until search fee is paid.	

2. Drawings:

☐ received:

☐ not received:

For International Bureau use only	
Date of receipt of the record copy by the International Bureau:	

Form PCT/RO/101 (last sheet) (July 1998; reprint January 2000) LegalStar 2000, Form PCTREQ See Notes to the request form

PATENT COOPERATION TREATY
APPOINTMENT OF AGENT

The undersigned applicant hereby appoints as agents:

TSEVDOS, Estelle J. (Reg. No. 31,145)
of
KENYON & KENYON
One Broadway
New York, New York 10004
United States of America

to represent the undersigned before all the competent International Authorities in connection with the following international application:

TITLE: COMPOSITION FOR IMPROVING SKIN LIPID BARRIER FUNCTION

APPLICANT'S OR AGENT'S FILE REFERENCE: 2870/250

INTERNATIONAL APPLICATION NO.: PCT/US00/08871

INTERNATIONAL FILING DATE: 04 April 2000

filed with the United States Receiving Office and to make or receive payments on its behalf.

APPLICANT: Daniel H. MAES

ADDRESS: 279A Nassau Road

Huntington, New York 11743

US

SIGNATURE:



DATE:

5/30/00

APPLICANT: Jon ANDERSON
ADDRESS: 3838 Briarpatch Circle
Galesburg, Michigan 49053
US

SIGNATURE: 

DATE: 6/3/00

APPLICANT: Kenneth D. MARENUS
ADDRESS: 62 McCulloch Drive
Dix Hills, New York 11746
US

SIGNATURE: 

DATE: 5/31/00

APPLICANT: Thomas MAMMONE
ADDRESS: 4 Spencer Street
Farmingdale, New York 11735
US

SIGNATURE: 

DATE: 5/30/00

CT/US 00/08871
RO/US 12 JUN 2000

APPLICANT: Christina G. FTHENAKIS

ADDRESS: 9 Lucille Lane

Dix Hills, New York 11746

US

SIGNATURE: 

DATE: 6/1/00

282617

PCT

FEE CALCULATION SHEET

Annex to the Request

For receiving Office use only

PCT/US 00/08871

International application No.

Applicant's or agent's
file reference **2870/250**

04 APR 2000 (04.04.00)
Date stamp of the receiving Office

Applicant
COLOR ACCESS, INC.

CALCULATION OF PRESCRIBED FEES

1. TRANSMITTAL FEE 240.00 T

2. SEARCH FEE 990.00 S

International search to be carried out by **EP**

(If two or more International Searching Authorities are competent in relation to the international application, indicate the name of the Authority which is chosen to carry out the international search.)

3. INTERNATIONAL FEE

Basic Fee

The international application contains **21** sheets.

first 30 sheets 427.00 b1

0 x **0.00** b2
remaining sheets additional amount

Add amounts entered at b1 and b2 and enter total at B 427.00 B

Designation Fees

The international application contains **84** designations.

8 x **92.00** = 736.00 D

number of designation fees amount of designation fee payable (maximum 8)

Add amounts entered at B and D and enter total at I 1,163.00 I

(Applicants from certain States are entitled to a reduction of 75% of the international fee. Where the applicant is (or all applicants are) so entitled, the total to be entered at I is 25% of the sum of the amounts entered at B and D.)

4. FEE FOR PRIORITY DOCUMENT (if applicable) P

5. TOTAL FEES PAYABLE 2,393.00

Add amounts entered at T, S, I and P, and enter total in the TOTAL box

TOTAL

☐ The designation fees are not paid at this time.

MODE OF PAYMENT

<input checked="" type="checkbox"/> authorization to charge deposit account (see below)	<input type="checkbox"/> bank draft	<input type="checkbox"/> coupons
<input type="checkbox"/> cheque	<input type="checkbox"/> cash	<input type="checkbox"/> other (specify):
<input type="checkbox"/> postal money order	<input type="checkbox"/> revenue stamps	

DEPOSIT ACCOUNT AUTHORIZATION *(this mode of payment may not be available at all receiving Offices)*

The RO/ US ☒ is hereby authorized to charge the total fees indicated above to my deposit account.

☒ *(this check-box may be marked only if the conditions for deposit accounts of the receiving Office so permit)* is hereby authorized to charge any deficiency or credit any overpayment in the total fees indicated above to my deposit account.

☐ is hereby authorized to charge the fee for preparation and transmittal of the priority document to the International Bureau of WIPO to my deposit account.

05-1320

04/04/00

Estelle J. Tsevdos
By: Mary C. Wilson, Reg. No. 30,333

Deposit Account No.

Date (day/month/year)

Signature **Estelle J. Tsevdos**

PCT

US

00/08871

GENERAL POWER OF ATTORNEY

(for several international applications filed under the Patent Cooperation Treaty)

(PCT Rule 90.5)

The undersigned person(s):

(Family name followed by given name; for a full legal entity, full official designation. The address must include postal code and name of country.)

COLOR ACCESS, INC.
7 Corporate Center Drive
Melville, New York 11747
US

hereby appoint(s) the following person as:

☒ agent

☐ common representative

Name and address

(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)

TSEVDOS, Estelle J.
Kenyon & Kenyon
One Broadway
New York, New York 10004
US

to represent the undersigned before

☒ all the competent International Authorities

☐ the International Searching Authority only

☐ the International Preliminary Examining Authority only

in connection with any and all international applications filed by the undersigned with the following Office

U S

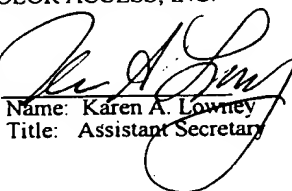
as receiving Office

and to make or receive payments on behalf of the undersigned.

Signature(s) *(where there are several persons, each of them must sign; next to each signature, indicate the name of the person signing and the capacity in which the person signs, if such capacity is not obvious from reading this power):*

COLOR ACCESS, INC.

By


Name: Karen A. Lowrey
Title: Assistant Secretary

Date:

Oct 22, 1998

RECEIVED

NOV 6 2001

TECH CENTER 1600 000

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau(43) International Publication Date
11 October 2001 (11.10.2001)

PCT

(10) International Publication Number
WO 01/74327 A1

- (51) International Patent Classification⁷: **A61K 7/48**
- (21) International Application Number: **PCT/US00/08871**
- (22) International Filing Date: **4 April 2000 (04.04.2000)**
- (25) Filing Language: **English**
- (26) Publication Language: **English**
- (71) Applicant (for all designated States except US): **COLOR ACCESS, INC.** [US/US]; 7 Corporate Center Drive, Melville, NY 11747 (US).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): **MAES, Daniel, H.** [FR/US]; 279A Nassau Road, Huntington, NY 11743 (US). **ANDERSON, Jon** [US/US]; 3838 Briarpatch Circle, Galesburg, MI 49053 (US). **MARENUS, Kenneth, D.** [US/US]; 62 McCulloch Drive, Dix Hills, NY 11746 (US). **MAMMONE, Thomas** [US/US]; 4 Spencer Street, Farmingdale, NY 11735 (US). **FTHENAKIS, Christina, G.** [US/US]; 9 Lucille Lane, Dix Hills, NY 11746 (US).
- (74) Agent: **TSEVDOS, Estelle, J.**; Kenyon & Kenyon, One Broadway, New York, NY 10004 (US).
- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.
- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).
- Published:**
— with international search report
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: COMPOSITION FOR IMPROVING SKIN LIPID BARRIER FUNCTION

(57) Abstract: The invention relates to a composition for topical application to the skin comprising effective amounts of a protease inhibitor and a cell differentiation enhancer. The composition is useful in promoting skin lipid barrier repair and maintaining the integrity of the lipid barrier. In this regard, the compositions can be used in the treatment and prevention of dry skin, and associated chrono/photo-aging conditions, in the treatment and prevention of irritation on the skin, in the treatment and prevention of UV-related damage to the skin, and in the enhancement of the retention of self-tanning.

WO 01/74327 A1

COMPOSITION FOR IMPROVING SKIN LIPID BARRIER FUNCTION

5 Field of the Invention

The invention relates to cosmetic and pharmaceutical compositions. More specifically, the invention relates to topical compositions that are useful in enhancing the function of the skin's natural lipid barrier.

10 Background of the Invention

15 Skin is typically characterized as consisting of three distinct layers, namely the stratum corneum, the epidermis and the dermis. The stratum corneum, the outermost layer, is made up of keratinized cells, surrounded by intercellular space filled with
20 lipids. The stratum corneum provides a substantial physical barrier to penetration of most substances to the lower layers of the skin. In addition to preventing transport of substances to the other skin layers, however, this barrier also aids in prevention of water loss from the skin. Both functions are
25 primarily attributable to the presence of the lipids in the stratum corneum.

There are two sources of the skin surface lipids making up this important barrier: sebaceous glands and the epidermis. The lipids are a diverse group of compounds, comprising triglycerides,
30 diglycerides, ceramides, free fatty acids, wax esters, cholesterol and cholesterol esters, and squalene. The quantity and composition of the skin surface lipids differ from place to place on the body, and may to some extent be related to the number of sebaceous glands in a given area of the skin. The condition of
35 the skin surface lipids may also be affected by an essential fatty acid deficiency. Additionally, the lipid barrier is easily diminished by exposure to harsh detergents or soaps. It is apparent, then, that the quality of the skin lipid barrier can vary widely, depending on a number of different factors, and therefore, may not always be adequate to perform its protective function optimally.

As an attempt to compensate for what may be a less than adequate lipid barrier, cosmetic compositions frequently incorporate components which compensate for water loss. Examples of such materials are hygroscopic humectants, e.g., urea or propylene glycol, which hold water on the skin; or emollients, e.g., oleyl alcohol or caprylic/capric triglycerides. Certain cosmetic components may be occlusive skin conditioners, which are used to provide an "artificial" barrier; such compounds are frequently lipids which remain on the skin surface, and include various hydrogenated oils, waxes and butters. Although many of these products provide an effective means of stemming water loss from the skin, they do have to be reapplied frequently to maintain the effect, and do not generally constitute a natural-occurring component of the stratum corneum, potentially giving rise to an unnatural, greasy feel to the skin. In addition, various pharmaceutical or cosmetic active agents are also frequently used to treat the symptoms of dry skin-associated conditions; however, in many cases, particularly with pharmaceutical agents, the treatments themselves may cause undesirable side effects in the individual being treated, while ultimately resulting in no actual repair of the lipid barrier.

The most desirable situation, from a functional point of view, is to find a way to enhance the skin's own ability to maintain and/or repair the strength of its barrier, so that the protective barrier formed is completely natural. It has now been discovered that a combination of specific skin active agents results in an unexpected increase in the strength of the natural barrier, by stimulating the production and maintenance of the barrier's naturally occurring components. There is thus provided a new type of cosmetic or pharmaceutical composition which functions by enhancing the skin's own functions, resulting in a more natural means of preventing dry skin and other undesirable results of a deficient lipid barrier.

Summary of the Invention

The invention relates to cosmetic and pharmaceutical compositions comprising lipid barrier-enhancing effective amounts of at least one protease inhibitor and at least one cellular differentiation enhancer. The composition can also comprise, in a preferred embodiment, effective amounts of a sterol sulfate, an at least one naturally occurring skin lipid component. The composition of the invention can be used in a method for strengthening the natural lipid barrier of the skin, as well as other methods of skin treatment that are made possible by the strengthening of the barrier.

Detailed Description of the Invention

The combined actives of the composition of the invention have been found to be highly effective in stimulating the repair of a damaged lipid barrier, and therefore, are shown to be useful as well in maintenance of a normal and healthy lipid barrier. For the purposes of the present invention and claims, these abilities will be referred to as strengthening the lipid barrier. The compositions of the invention can strengthen the lipid barrier at least about 40%, relative to a placebo control, as measured by a reduction of transepidermal water loss (TEWL) after a barrier challenge, a standard measurement of barrier function. Preferably, the compositions are capable of reducing TEWL at least about 50%, more preferably at least about 60%, and most preferably at least about 70%. The invention incorporates as essential elements a protease inhibitor and a cellular differentiation enhancer. Protease inhibitors are compounds, usually naturally occurring, which inhibit the action of proteases in the skin. Skin proteases also occur naturally, and, among other effects, are involved in the breaking down of the collagen and elastin that is required to maintain the healthy appearance of skin. In the present case, the protease inhibitors used in the invention are thought to act by preventing the breakage of the desmosome bond

between corneocytes at the skin surface, thereby keeping the outer layer of skin cells intact, in essence delaying desquamation. This skin layer provides a barrier to water loss, and the enhanced retention of the barrier by the delay of desquamation provides
5 reinforces this barrier to the loss of water further. A variety of protease inhibitors are known. Examples of useful protease inhibitors include, but are not limited to, triterpenoid-containing extracts and refined compounds, for example, white birch bark extract, silver birch bark extract, *Boswellia* extract,
10 bearberry extract, *Centella asiatica* extract, or *Pygeum* (*Prunus africanum*) extract and individual protease inhibitor compounds that may be present in these extracts, including betulinol (betulin), betulinic acid, boswellic acid, ursolic acid, oleanolic acid, oleanol, asiaticoside, asiatic acid, and madagassic acid;
15 phenolic-containing extracts, such as green tea extracts and apple extracts, and compounds contained therein, such as EGCG, ECG, catechins, phenylpropanoids, and phloretin; protein-based extracts, such as soy protein, or egg protease inhibitors, or cholesterol sulfate and phytosterol sulfates. Preferred protease
20 inhibitors are triterpenoids, particularly boswellic acid, betulinol, and betulinic acid, or extracts containing same in substantial quantities.

It will be recognized from the foregoing that either an
25 extract or the individual protease inhibitor can be used, and that the individual protease inhibitors can also be found in other types of extracts. The amount of active material used will vary depending upon the whether an extract or isolated compound is used, the concentration of active material in a given extract, and
30 the known potency of the active material. However, the concentration of active protease inhibitor in the final product should generally be between about 0.001 to about 10%, preferably

about 0.05 to about 5%, more preferably about 0.1 to about 1%, by weight of the total composition.

The second component is a cellular differentiation enhancer. Such compounds act in the present invention to increase the ability of the relevant epidermal cells to synthesize the lipids that constitute the primary component of the barrier. The epidermal cells that produce lipids do not do so during their entire life cycle, however, but do so only at the point of differentiation. If this differentiation is delayed to the point at which the epidermal cells reach their terminal point in migration to the skin surface, the production of lipids is concurrently delayed, and therefore, their effect, if any, is diminished. The differentiation enhancers used in the invention stimulate the earlier production of lipids from epidermal cells, thereby increasing the length of time over which the lipids are being produced, and presumably concurrently increasing the lipid content of the barrier. Several types of cellular differentiation inhibitors are known, and these include, but are not limited to sclareolide, forskolin, 7-dehydrocholesterol, and Vitamin D3 analogs. The differentiation enhancer also will be used in amount consistent with its known activity, 0.001 to 10%, preferably about .0025 to about 5%, more preferably about 0.05 to about 1%, by weight of the total composition.

The combination of the protease inhibitor and the differentiation enhancer is shown to have a strong effect on barrier repair when compared with control vehicles and with other compounds commonly used in skin enhancement. Specifically, on skin that had been challenged with tape stripping, it was found that combination of these two components exhibits about a 50% increase in barrier repair, as measurable by transepidermal water loss, in comparison with the placebo, after a period of three days. Thus, this combination on its own is shown to be able to increase barrier function substantially.

Although the noted combination is highly effective on its own, it has been further shown that the combination achieves even

further enhancement of barrier function by its combination with certain other skin enhancement compounds. More specifically, the combination with one or more of certain specific skin enhancers. In a preferred embodiment, the barrier repair combination is further combined with cholesterol sulfate, which in the present specification and claims is intended to refer to the corresponding plant-derived material, phytosterol sulfate. Cholesterol sulfate, as described in Applicants' copending application serial no. 09/246,607, incorporated herein by reference, also has an effect on the skin, by increasing the cohesion of the stratum corneum. Thus, its combination with the protease inhibitor/differentiation enhancer even further strengthens the ability of the composition maintain the integrity of the stratum corneum. The amount of cholesterol sulfate employed is preferably about 0.05 to about 10%, preferably from about 0.5 to about 5%, most preferably about 1 to about 3%, by weight of the total composition.

In all formulations in which cholesterol sulfate is employed, and in a particularly preferred embodiment, it is preferred that the composition also contain other components of the naturally occurring lipid barrier. In a particularly preferred embodiment, the cholesterol sulfate is combined with at least one of each of fatty acids, ceramides, and a sterol, preferably cholesterol or phytosterol. Fatty acids may be up to 24 carbon atoms in length. Examples of preferred fatty acids include butyric acid, caproic acid, octanoic acid, decanoic acid, dodecanoic acid, tetradecanoic acid, palmitic acid, stearic acid, linoleic acid and oleic acid. Particularly preferred are fatty acids with a C₁₂ to C₂₀ chain length.

The ceramides to be employed in the compositions of the invention are sphingolipids, having a sphingosine or related molecule backbone with fatty acids or ω -esterified fatty acids linked to an amino group on the sphingosine, and in some cases, with saccharide moieties linked to the terminal hydroxyl of the sphingosine. In particular, the compositions may contain ω -esterified ceramides or acylceramides, cerebrosides, ω -esterified cerebrosides, or acylglycosyl sphingolipids. Particularly

preferred types of ceramides for the present compositions are ceramide III and cerebrosides.

In those compositions in which cholesterol sulfate is combined with these lipids, the lipid components each can be used
5 in an amount of from about 0.05 to 10%, preferably 0.5 to about 5%, most preferably about 1 to about 3%, all by weight of the total composition. In a particularly preferred embodiment, the cholesterol sulfate and the lipid components are present in substantially equal amounts in the composition. It will be
10 understood from the foregoing that the lipid component need not be pure lipid, but rather may be natural extracts containing one or more desirable lipids, and used in amounts consistent with attaining the concentrations recommended above.

The effect of the present compositions in effecting barrier
15 repair or maintaining the integrity of the skin's outer layer can be applied to a number of different uses. For example, the compositions can be used to treat any condition in which a deficient or faulty barrier is a factor. In this regard, the compositions can be used to improve the long term moisture
20 retention of the skin, or in prevention or treatment of dry skin conditions generally, or specific dry skin conditions, such as result from regular exposure to detergents, soaps and hot water; seasonal exposure to harsh weather conditions, e.g., cold, wind and/or sun; occupational exposure to harsh chemicals or other
25 drying or damaging agents; or pathological conditions such as eczematous dermatides, psoriasis, ichthyoses, xerosis and the like. It is also well-known that dry skin is commonly associated with aging(both intrinsic and photoaging), and the compositions can be used in prevention of further damage to aging skin, or
30 treatment and/or reversal of already present damage, including the appearance of fine lines and wrinkles, which are frequently associated with dry skin and the thinning of the stratum corneum that occurs with age. The compositions can also be used in the treatment of a defective skin barrier, such as occurs on the soles
35 of the feet, and palms of the hands, where the stratum corneum is very thick, but the lipid barrier is poor. In addition, defective

skin barriers frequently occur in association with burns, wounds, blisters, stasis ulcers and bedsores; such injuries can be expected to benefit from application of the compositions.

5 A further use of the compositions of the invention is in reduction of the skin's response to irritants and sensitizers. A significant percentage of the population considers itself to have sensitive skin, in that they perceive a frequent, stinging or painful response to various elements to which the skin may be exposed, be it through makeup or skin care products, environmental
10 stimuli such as smoke or pollution, or occupational exposure to chemicals. In addition, even normal skin can have a reaction to exposure to known irritants, such as acids. As it is well known that the stratum corneum and lipids constitute the first line of defense against irritants, by providing a physical barrier to
15 permeability of such materials to the lower skin layers, the application of the compositions of the invention, by increasing the integrity of the barrier, can reduce the reactivity of the skin of both normal and sensitive individuals to irritants and sensitizers. In one embodiment, for example, the compositions can
20 be used to reduce the reaction of the skin to the irritation caused by therapeutic acids such as alpha and beta hydroxy acids, retinoic acid, and the like, or to reduce the irritation caused by insect bites or stings, or alleviate the irritation experienced with contact dermatitis.

25 The increased cohesion of the stratum corneum brought about by the compositions of the invention also provides other benefits. The stratum corneum represents an important physical barrier between the environment and the deeper skin layers as well as the internal organs. The presence of this thicker layer thus will
30 provide a greater level of protection than is possible with weaker barrier. Perhaps the most important aspect of this effect is the enhanced self-protection from UV rays. The thicker stratum corneum means an increase in the Minimal Erythema Dose of UV which will result in sunburn or more serious skin damage. In
35 connection with this aspect of the invention, the components of the invention may be beneficially combined with one or more

sunscreens for an enhanced UV protective composition which provides both short- and long-term protection. Thus, the invention provides sunscreen compositions comprising effective amounts of the components of the composition of the invention, and one or more sunscreens. Examples of useful sunscreens include, but are not limited to, inorganic sunscreens such as titanium dioxide, zinc oxide, and iron oxide; and organic sunscreens, such as camphor derivatives, cinnamates, salicylates, benzophenones, triazines, PABA derivatives, diphenylacrylate derivatives, and dibenzoylmethane derivatives. In such sunscreen compositions, the components of the invention are present in the amounts described above, and the respective sunscreens are present in the amounts normally used for UV protection.

An additional use of the compositions of the invention is in the enhancement and prolongation of self-tanning products. One of the recognized limitations of self-tanners, which are normally based on dihydroxyacetone (DHA) as the active component, is that the tan on the skin lasts only as long as the skin cells receiving the DHA remain in place. In the normal course of events, then, a self-applied tan usually lasts no more than 5 days, i.e., for as long as it takes for the stratum corneum layer to which the DHA was applied to fully turn over. When the compositions of the invention are combined with DHA, or any other self-tanning agent, in a typical self-tanning formulation, however, the rate of turnover of the stratum corneum to which the composition is applied is slowed down, thereby permitting a longer rate of retention of the "tanned" cells, and thus prolonging the length of time the tan remains visible on the skin. Thus, the invention provides a self-tanning composition comprising a protease inhibitor, a cell-differentiation enhancer, and an effective amount of a self-tanning agent, optionally containing cholesterol sulfate and the lipid component. In a preferred embodiment, the self-tanner is DHA, which is usually applied in an amount of from about 2.5 to about 10% by weight of the formulation. The self-tanner may also be imidazole, preferably in combination with DHA, in an amount of about 1-10%, preferably about 1.5-7.5%.

The compositions of the invention are employed in a manner appropriate to the intended final use of the product. For example, in the treatment of occasional dry skin due to exposure to weather or other temporary conditions, or in the treatment of occasional skin irritation, the compositions can be used on an as-needed basis until the condition is relieved. When being used to treat a more permanent condition, for example, a condition associated with a defective or deficient lipid barrier, particularly sensitive skin, dry skin associated with any type of aging, or the wrinkling or fine lines associated with a thinning of the stratum corneum with aging, the composition is preferably applied chronically, to prevent recurrence of the condition. For this purpose, it is suggested as an example that topical application of the composition, in an amount of from about 0.1 mg/cm² to 2 mg/cm² of skin, be performed from about once per week to about 4 or 5 times daily, preferably from about 3 times a week to about 3 times daily, most preferably about once or twice per day. By "chronic" application, it is meant herein that the period of topical application may be over the lifetime of the user, preferably for a period of at least about one month, more preferably from about three months to about twenty years, more preferably from about six months to about ten years, more preferably still from about one year to about five years, thereby resulting in the treatment or prevention of the condition in question.

When the composition is used in conjunction with a sunscreen, it is applied in the same amounts as specified above, on an as-needed basis, to mitigate the effects of exposure to the sun. When used in combination with a self-tanner, the composition is also applied in similar amounts, on the portion of the skin to be tanned, with repetition, again, on an as-needed basis.

The invention is further illustrated by the following non-limiting examples:

EXAMPLES

Example 1.

5 A study is conducted to determine the efficacy of certain compositions in enhancing repair of the lipid barrier. Female volunteers with normal skin, who are in good general health, free of any dermatological disorders, participate in the study. Their skin barrier is challenged by tape stripping according to the procedure outlined below. After their evaluation, the subjects receive a treatment every day on the right side of their face. They are also given the product containing the actives to use once every night for three nights, on the right side of the face only, the left side being the untreated control side. A separate group is given a placebo, without actives, as treatment product.

10 To challenge the barrier, the subjects are acclimated in an environmental room at 40% relative humidity and 70°C for 15-20 minutes. A 5 cm by 1cm area is marked on the lower right cheek near the jaw line and initial water evaporation measurements are taken in three separate spots approximately 1 cm apart in a row. Five cm of cello-tape is placed on the skin in the outlined area, starting from the top of the cheek and after one firm stroke in each direction it is removed by gently pulling in a downward direction parallel to the skin. The procedure is repeated and water evaporation is measured after every five strips until the barrier is disrupted as indicated by a minimum of 18g/sq.m hr on one of the three spots. Both sides of the face are stripped in the same way. The subjects returned for TEWL evaluation 1,2 and 3 days after tape stripping of the skin to monitor the repair.

20 25 30 35 Barrier repair is evaluated by first challenging the skin as described above. One side is product-treated 2 times a day, and the other is the untreated control. Repair is measured in the increase in the recovery of the skin on the stripped and treated site compared to the stripped untreated site. From this, total

repair is calculated over three days by calculating the change in the area parameter. The smaller the area, the faster the repair.

Treatment products are (1) a composition containing 0.1% sclareolide and 0.2% white birch extract; (2) a composition containing 0.1% sclareolide and 0.2% boswellic acid; (3) a composition containing .2% each of phytocohesine (phytosterol sulfate), cennamides (wheat-derived ceramides), boswellic acid, cholesterol, and linoleic acid, and .1% sclareolide. The results obtained indicate for composition (1), barrier repair is 50% over placebo; for composition (2), repair is 59% over placebo, and composition (3) shows barrier repair at 78% over the placebo, each composition therefore showing substantial efficacy in barrier repair.

What we claim is:

1. A composition for topical application to the skin comprising effective amounts of at least one protease inhibitor and at least one cell differentiation enhancer.

2. The composition of claim 1 in which the protease inhibitor is selected from the group consisting of triterpenoid-containing extracts, and active components thereof, phenolic-containing extracts and active components thereof, and protein-based extract and active components thereof.

3. The composition of claim 1 in which the protease inhibitor is selected from the group consisting of white birch extract, silver birch extract, *Boswellia* extract, bearberry extract, *Centella asiatica* extract, *Pygeum* (*Prunus*) *africanum* extract, betulinol, betulinic acid, boswellic acid, ursolic acid, oleanolic acid, oleanol, asiaticoside, asiatic acid, madagassic acid, green tea extract, apple extracts, EGCG, ECG, catechins, phenylpropanoids, phloretin, soy protein, egg protease inhibitors, cholesterol sulfate, phytosterol sulfate, and combinations thereof.

4. The composition of claim 3 in which the protease inhibitor is selected from the group consisting of white birch extract, betulinol, betulinic acid, *Boswellia* extract, boswellic acid, and combinations thereof.

5. The composition of claim 1 in which the cell differentiation enhancer is selected from the group consisting of forskolin, sclareolide, 7-dehydrocholesterol, and Vitamin D3 analogs.

6. The composition of claim 5 in which the enhancer is sclareolide.

7. The composition of claim 1 comprising about .001 to about 10% of a protease inhibitor and about 0.001-10% cell differentiation enhancer.

5 8. The composition of claim 1 comprising about 0.1 to about 1% of a protease inhibitor and about .05-1% cell differentiation enhancer.

10 9. The composition of claim 8 in which the inhibitor is white birch extract, betulinol, or boswellic acid and the enhancer is sclareolide.

15 10. The composition of claim 1 which also contains cholesterol sulfate.

11. The composition of claim 10 which also contains at least one fatty acid, at least one ceramide, and at least one sterol.

20 12. The composition of claim 11 in which the fatty acid is a C12-C20 fatty acid.

25 13. The composition of claim 11 containing about 0.05 to 10% of each of cholesterol sulfate or phytosterol sulfate, fatty acid, ceramide, and sterol.

14. The composition of claim 1 which further comprises an effective amount of at least one self-tanning agent.

30 15. The composition of claim 14 in which the self-tanning agent is DHA.

16. The composition of claim 1 which further comprises at least one sunscreen.

35 17. A method for treatment or prevention of dry skin which comprises applying to the skin a composition according to claim 1.

18. A method for treatment or prevention of dry skin which comprises applying to the skin a composition according to claim 9.

5 19. A method for treatment or prevention of dry skin which comprises applying to the skin a composition according to claim 11.

10 20. A method for reducing or preventing skin's response to irritants or sensitizers comprising applying to the skin a composition of claim 1.

15 21. A method for reducing or preventing skin's response to irritants or sensitizers comprising applying to the skin a composition of claim 9.

22. A method for reducing or preventing skin's response to irritants or sensitizers comprising applying to the skin a composition of claim 11.

20 23. A method for protecting skin against effects of exposure to UV radiation comprising applying to the skin a composition of claim 1.

25 24. A method for protecting skin against effects of exposure to UV radiation comprising applying to the skin a composition of claim 9.

30 25. A method for protecting skin against effects of exposure to UV radiation comprising applying to the skin a composition of claim 11.

35 26. A method for protecting skin against effects of exposure to UV radiation comprising applying to the skin a composition of claim 16.

27. A method for tanning the skin without exposure to the sun comprising applying to the skin a composition according to claim 14.

5 28. A method for tanning the skin without exposure to the sun comprising applying to the skin a composition according to claim 15.

5000
09554984

INTERNATIONAL COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 2870/250	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/US 00/08871	International filing date (day/month/year) 04/04/2000	(Earliest) Priority Date (day/month/year)
Applicant COLOR ACCESS INC		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☐ None of the figures.

INTERNATIONAL SEARCH REPORT

Inter Application No
PCT/US 00/08871

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K7/48

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

WPI Data, PAJ, EPO-Internal, MEDLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 99 62481 A (GUERLAIN S.A. ET AL.) 9 December 1999 (1999-12-09) page 3, line 21 -page 4, line 26 example 3 ---	1,3,5,16
A	EP 0 976 396 A (L'OREAL) 2 February 2000 (2000-02-02) claims 13,15 ---	1,3,5
A	WO 99 24009 A (LVMH RECHERCHE ET AL.) 20 May 1999 (1999-05-20) page 8, line 3 page 8, line 7 page 8, line 19 ---	1,3,5
A	WO 95 25524 A (LVMH RECHERCHE) 28 September 1995 (1995-09-28) claims 1-4,7 ---	1,3,5
-/--		

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

G document member of the same patent family

Date of the actual completion of the international search

5 December 2000

Date of mailing of the international search report

12/12/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Alvarez Alvarez, C

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/08871

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 99 63978 A (R.J.REYNOLDS TOBACCO COMPANY ET AL.) 16 December 1999 (1999-12-16) claim 12	6
A	EP 0 717 983 A (UNILEVER PLC ET AL.) 26 June 1996 (1996-06-26) page 3, line 10 - line 16	4

INTERNATIONAL SEARCH REPORT

Information on patent family members

Inter

Application No

PCT/US 00/08871

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
WO 9962481	A	09-12-1999	NONE		
EP 976396	A	02-02-2000	FR 2781670 A		04-02-2000
			JP 2000080016 A		21-03-2000
WO 9924009	A	20-05-1999	FR 2770776 A		14-05-1999
			EP 1028705 A		23-08-2000
WO 9525524	A	28-09-1995	FR 2717389 A		22-09-1995
			CN 1146153 A		26-03-1997
			EP 0751777 A		08-01-1997
			JP 10500395 T		13-01-1998
			US 5747538 A		05-05-1998
WO 9963978	A	16-12-1999	AU 3902299 A		30-12-1999
EP 717983	A	26-06-1996	US 5529769 A		25-06-1996
			CA 2164050 A		21-06-1996
			JP 8208424 A		13-08-1996